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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,811	12/02/2003	Craig Basson	955-12 DIV	3344

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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	**PAPER NUMBER**
1642	
MAIL DATE	**DELIVERY MODE**
11/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/725,811	BASSON, CRAIG	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *01 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *23,25,26,28,29,31 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *23, 25, 26, 28, 29, 31, 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The Amendment filed October 1, 2007 in response to the Office Action of April 30, 2007 is acknowledged and has been entered. Previously pending claims 24, 27, 34 have been canceled, claim 23 has been amended. Claims 23, 25, 26, 28, 29, 31, 33 are pending and are currently being examined.

2. The following objections are being maintained:

Objection to the Specification is maintained.

Applicant argues that descriptions of the figures are found at pages 28 and 29 and page 32 of the specification. The argument has been considered but has not been found persuasive because the figures are required to be fully described either in the Brief Description of the Drawing or on the Figures themselves. Disclosure of the meaning of the figures embedded in the body of the specification is not sufficient to meet the formal requirements for the description of the figures. Amendment of either the Brief Description or the Drawings themselves is required.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 23, 25, 26, 28, 29, 31, 33 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed April 30, 2007, Section 6, pages 2-7.

Applicant argues that Examiner Ungar, in the interview of July 19, 2007, explained that upon further review of the application, limiting the claims to the two

disclosed species is not necessary to overcome the present rejection and that amending the claims to recite "a translated human 5' T-box sequence of TBX5" would suffice to overcome the rejection. The argument has been considered but has not been found persuasive because the summary of the interview in the instant case states specifically "Discussed rejections of record. Applicant will submit arguments, amendments and/or declaration for consideration." The interview summary does not state that amendment of the claim to insert the term "human" would overcome the rejection. Had examiner made this determination, it would have been included in the summary of the interview. The amended claims have been considered, as the summary indicated that they would, and have not been found to overcome the grounds of rejection under the written description requirements, wherein as previously set forth, the specification teaches that the human TBX5 protein is SEQ ID NO: 1 (para 0022). The human wild-type TBX5 protein includes a T-box sequence that begins with amino acid 56 and ends with amino acid 238 of the human protein of SEQ ID NO: 1 and teaches that a useful 5' T-box sequence capable of binding to the major groove of target DNA begins at approximately amino acid 56 of the human protein of SEQ ID NO: 1 and contains a sufficient number of residues to inhibit cellular proliferation. Although the rejection clearly states, at paragraph 0024 that the wild-type human protein is SEQ ID NO:1, the instantly claimed invention is **not** drawn to the wild-type polypeptide, it is not drawn to **a** (emphasis added) 5' T-box sequence capable of binding to the major groove of target DNA which begins at approximately amino acid 56 of the human protein of SEQ ID NO: 1 and contains a sufficient number of residues to inhibit cellular proliferation, a property disclosed as critical, in the specification as originally filed, to the function of the claimed invention. The

instantly claimed invention is drawn to "**a** (emphasis added) translated human 5' T-box sequence capable of binding to the major groove of target DNA", wherein a sufficient number of residues is neither required nor taught other than the two species exemplified. Thus the claims read on not only the wild-type, but also allelic variants and mutated translated human 5' T-box sequences capable of binding to the major groove of target DNA, wherein the specification provides no information drawn to the "sufficient number of residues required", provides no information drawn to those translated human 5' T-box sequences capable of binding to the major groove of target DNA that inhibit the proliferation of a cell other than the full length wild-type or the fragment of the full length wild-type exemplified in the specification as originally filed.

As specifically set forth previously, the instant specification may provide an adequate written description of the introduced nucleic acid encoding a polypeptide comprising a translated 5' T-box sequence of TBX5, as defined by the specification, wherein said polypeptide contains a sufficient number of binding residues and is capable of binding to the major groove of target DNA which will inhibit the proliferation of a cell/malignant cell by meeting the requirements of 35 USC 112, first paragraph as interpreted in Lilly and Enzo. For the reasons set forth previously and above, the claimed invention does not meet these requirements and therefore the claims properly remain rejected under 35 USC 112, first paragraph written description.

The arguments have been considered but have not been found persuasive and the rejection is maintained.

6. Claims 23, 25, 26, 28, 29, 31, 33 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed April 30, 2007, Section 7, pages 7-11.

Applicant argues that in the interview of July 19, 2007 Examiner acknowledged that the application discloses *in vivo* studies performed in normal chick embryos and stated that in order to overcome the enablement rejection she would like to see additional objective evidence showing a nexus between the chick embryo studies and a recognized animal model in mouse, wherein she explain that the nexus should evidence chick embryo studies as being predictive of studies in the animal model. Applicant submits Chambers et al (In Vivo, 1990, 4(4):215-219) wherein the abstract states (1) "a good correlation" exists between chick embryo assays and nude mice for measuring metastatic properties of different cell types from different species and (2) the abstract further states that the chick embryo assay is a useful alternative host for metastasis studies and that it correlates well with assays using nude mice.

The argument has been considered but has not been found persuasive because the data presented in the reference is not commensurate in scope with the instantly claimed invention wherein the instantly claimed invention is not drawn to metastases studies but rather is drawn to the in vivo inhibition of proliferation of a cell wherein the claims read on the *in vivo* treatment of cancer. Further, although the abstract indeed states that a "good correlation" exists, had Applicant read further in the reference Applicant would have noted that Chambers et al specifically teach that "it must be stressed that the metastasis assay described here, using chick embryos **CANNOT BE USED SOLELY AND INSTEAD OF ASSAYS IN MICE** (emphasis added).....the chick embryo assay **MAY IN**

SOME CASES (emphasis added) reduce the numbers of mice required for these studies." (see p. 217, col 2). Thus it is clear that even in metastasis assays, the information from chick assays can not predictably be substituted for that in the animal model, wherein the cases where the assay might be useful are not defined in any limiting manner. The reference specifically identifies a set of cell lines whose metastatic potential could not be distinguished in the chick assay wherein it could be distinguished in the animal model. Thus it is clear that it is not possible to predictably distinguish, with a reasonable expectation of success which metastatic cells will be metastatic in not only the chick assay but also the animal model. This is clearly the reason for the strong statement set forth above on page 217, column 2 and clearly casts doubt on the summary statement in the abstract which might have more responsibly read that there is a "good correlation" in some cases.

The reference further teaches at page 218, col 1, that disadvantages of the chick embryo assay should be considered. In particular, the reference suggests that tumorigenicity and subsequent spontaneous metastasis from the tumor are better tested in assays in mice. This is clearly a point critical to the *in vivo* testing of inhibition of proliferation therapeutics. Although this sort of assay has been used with success by some groups using the chick embryo, "in our experience, the creation of "primary" tumors on the CAM surface of the chick embryo is subject to large variability which depends in part on damage induced on the CAM surface during experimental manipulation." Thus, given the above, given the contradictory results reported by the instant reference and others in the field, it appears that the use of the chick assay, even in the production of tumors, is called into question. Thus, if the production of the tumors is called into question, the use of the assay for identifying inhibitors of proliferation is also called into question and the instant

reference does not provide a reasonable nexus between the chick assay presented in the instant specification and conventional animal models predictive of efficacy of treatment *in vivo*.

It is noted for Applicant's convenience and to clarify the record, that Examiner specifically called into question the nexus between the chick assay and predictive animal models. Examiner did not state that she would like to see additional objective showing a nexus between the chick embryo studies and a recognized animal model in mouse, but rather that submission of objective evidence commensurate in scope with the claimed invention might be useful in overcoming the instant rejection.

Applicant submits Sausville et al (Cancer Res., 2006, 66:3351-3354) that discloses that mouse models of cancer have consistently been used to qualify new anticancer drugs for study in human clinical trials. The submission has been considered but has not been found persuasive to overcome the rejection. Although Examiner agrees that appropriate animal models, commensurate in scope with the claimed invention have consistently been used to qualify new anticancer drugs and are used conventionally to enable claims drawn to treatment of cancer with novel drugs, no data drawn to the instantly claimed invention, assayed in a mouse model has been submitted. For the reasons set forth above, the submitted Chambers et al reference does not provide a nexus between the instant chick assay and mouse models and therefore the information in the Sausville et al reference is not relevant.

Applicant argues that a well-accepted intersection exists between embryogenesis and oncogenesis and submits six abstracts, apparently to prove this intersection. The abstracts have been noted but the information in the references cannot be evaluated given that the entire references have not been submitted. The

problem with abstract submission is clearly demonstrated by the differences between the abstract of the Chambers et al reference, as set forth above, and the body of the reference. Further, even if the references are submitted in full and even if the references demonstrate the intersection between embryogenesis and oncogenesis, the references are still not commensurate in scope with the claimed invention wherein the instantly claimed invention is not drawn to the intersection of embryogenesis and oncogenesis but rather is drawn to the in vivo inhibition of proliferation of a cell wherein the claims read on the in vivo treatment of cancer.

The arguments have been considered but have not been found persuasive and the rejection is maintained.

7. It is noted that Applicant states that "For the foregoing reasons, the cited references individual or in combination fail to obviate the claimed invention". It is noted for Applicant's convenience that the rejections of record do not include any rejections under 35 USC 103. Further, Applicant has not discussed any of the references cited in the rejections under 35 USC 112, first paragraph in the previous office action.

New Grounds of Objection

8. Claim 26 is objected to because it does not further limit claim 23 from which it depends.

9. No Claims allowed.

10. All other objections and rejections set forth in the previous action are hereby withdrawn.

11. Applicant's amendment necessitated the new grounds of objection. Thus, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898. The fax phone number for this Art Unit is (571) 273-8300.

Susan Ungar
Primary Patent Examiner
October 30, 2007